

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P11066PC	<b>FOR FURTHER ACTION</b> <small>See Form PCT/IPEA/416</small>	
International application No. PCT/DK2004/000679	International filing date (day/month/year) 08.10.2004	Priority date (day/month/year) 22.10.2003
International Patent Classification (IPC) or national classification and IPC A61K31/4184, C07D235/14, C07D407/06, C07D409/06, A61P31/04		
Applicant ARPIDA A/S		

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> <i>sent to the applicant and to the International Bureau</i> a total of sheets, as follows:</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</li> <li><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</li> </ul> <p>b. <input type="checkbox"/> <i>(sent to the International Bureau only)</i> a total of (indicate type and number of electronic carrier(s)), containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>
<p>4. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li><input checked="" type="checkbox"/> Box No. I Basis of the opinion</li> <li><input type="checkbox"/> Box No. II Priority</li> <li><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li><input type="checkbox"/> Box No. IV Lack of unity of invention</li> <li><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li><input type="checkbox"/> Box No. VI Certain documents cited</li> <li><input type="checkbox"/> Box No. VII Certain defects in the international application</li> <li><input type="checkbox"/> Box No. VIII Certain observations on the international application</li> </ul>

Date of submission of the demand 19.08.2005	Date of completion of this report 07.12.2005
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Bérillon, L Telephone No. +49 89 2399-7078



INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITYInternational application No.  
PCT/DK2004/000679

## Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
  - This report is based on translations from the original language into the following language, which is the language of a translation furnished for the purposes of:
    - international search (under Rules 12.3 and 23.1(b))
    - publication of the international application (under Rule 12.4)
    - international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

## Description, Pages

1-60 as originally filed

## Claims, Numbers

1-37 as originally filed

- a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3.  The amendments have resulted in the cancellation of:
  - the description, pages
  - the claims, Nos.
  - the drawings, sheets/figs
  - the sequence listing (*specify*):
  - any table(s) related to sequence listing (*specify*):
4.  This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
  - the description, pages
  - the claims, Nos.
  - the drawings, sheets/figs
  - the sequence listing (*specify*):
  - any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
  - the entire international application,
  - claims Nos. 32, 33
    - because:
    - the said international application, or the said claims Nos. 32, 33 relate to the following subject matter which does not require an international preliminary examination (specify):  
**see separate sheet**
    - the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
    - the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
    - no international search report has been established for the said claims Nos.
    - the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	<input type="checkbox"/> has not been furnished
	<input type="checkbox"/> does not comply with the standard
the computer readable form	<input type="checkbox"/> has not been furnished
	<input type="checkbox"/> does not comply with the standard
- the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- See separate sheet for further details

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims	1-37
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-37
Industrial applicability (IA)	Yes: Claims	1-31, 34-37
	No: Claims	

**2. Citations and explanations (Rule 70.7):**

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
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(SEPARATE SHEET)**

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**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 32 and 33 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1 Prior art**

Reference is made to the following documents:

D1: WO 02/41886  
D2: WO 00/61134  
D3: WO 96/33176

**2 Novelty (Article 33(2) PCT)**

The present compounds differ from the compounds disclosed in D1-D3 at least in view of the definition of their substituent -COR<sub>3</sub>. The subject-matter of the present application is novel.

**3 Inventive step (Article 33(3) PCT)**

In view of closest prior art D1 the technical problem underlying the present application is regarded as the provision of further compounds useful as polypeptide deformylase (PDF) inhibitors for treating bacterial and parasitic infections. In communication dated 19.08.2005, page 2 second paragraph the Applicant states that the ability to inhibit bacterial polypeptide deformylase is only mentioned in D1 as a possible mechanism

and that no PDF inhibition are shown for the compounds of D1. In D1, page 3, second paragraph the mechanism is only postulated indeed. However, although a discovery of a mechanism may be an important piece of scientific knowledge, it cannot be considered as a technical contribution to the art. It is only the therapeutic effect of a molecule i.e. in the present case treating specific bacterial and parasitic infections, which is relevant for the assessment of inventive step within the meaning of Article 33(3) PCT.

In view of the structure of the compounds disclosed in D1, the present compounds appear to be obvious solutions to the posed technical problem. In communication dated 19.08.2005 the Applicant listed various points of differentiation between the present compounds and the examples disclosed in D1.

- The X group of the present compounds is first cited as point of differentiation. Although all the examples of D1 have a -N(OH)CHO group, the definition of Z in D1, claim 1 reads "N(OH)CHO or -CONHOH". Hence, the definition of X in the present compounds overlaps with the definition of Z in D1 and therefore cannot be the basis for inventive step.
- The same applies for the points of differentiation marked by the Applicant as \*, \*\* and \*\*\*. In D1, claim 1, R<sub>2</sub> can be H which results equally in a methylene group in said position \* and the positions marked \*\* and \*\*\* (positions 4 and 7 of the benzimidazole ring) can in the D1 compounds as in the present compounds be unsubstituted.
- The definition of R<sub>1</sub> in the present compounds overlap with the definition of R<sub>3</sub> in D1, claim 1.

The substituent in position 5 of the benzimidazole ring appears therefore to be the only distinguishing structural feature. In the present compounds, said substituent is restricted to -COR<sub>3</sub> with R<sub>3</sub> being -NHCH(R<sub>4</sub>)COR<sub>5</sub>, -NR<sub>6</sub>R<sub>7</sub>, -NHR<sub>7</sub> or -OR<sub>7</sub>. In D1, said substituent can be extremely varied (see definition of R<sub>5</sub> and R<sub>6</sub> in D1, claim 1) and equally includes amides or ester groups CONHR<sup>A</sup>, CONR<sup>A</sup>R<sup>B</sup>, CO<sub>2</sub>R<sup>A</sup>. Even if no exemplified compounds of D1 have said amide or ester groups, D1 taken as a whole clearly teaches that said ester or amide groups can be present in position 5 of the benzimidazole without jeopardizing the inhibitory activity of the resulting products. Hence, present compounds of formula (I) (at least those wherein R<sub>3</sub> is -NR<sub>6</sub>R<sub>7</sub>, -NHR<sub>7</sub> or -OR<sub>7</sub>) are obvious solutions to the problem of providing further compounds useful as PDF inhibitors. For these compounds the technical problem has to be seen as the provision of PDF inhibitors having an improved or unexpected effect over D1 which is not apparent yet.

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**4 Industrial applicability (Article 33(4) PCT)**

For the assessment of the present claims 32 and 33 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.